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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHOI, FRANK I	
ART UNIT	PAPER NUMBER
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/214,848	SEKINE, TERUAKI	
	Examiner	Art Unit	
	FRANK I. CHOI	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/18/2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13,14,19-27,31,32,34 and 36-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,14,19-27,31,32,34 and 36-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 12/18/2008 has been entered.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 13,14,19-27,31,32,34,36-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ochoa et al. (US Pat. 5,296,353) in view of Babbit et al. (US Pat. 5,766,920), Ochoa et al. (U.S. Pat. 5,443,983), the acknowledged prior art and Sekine et al.

Ochoa et al. (US Pat. 5,296,353) teach activation of autologous T-lymphocytes with anti-CD3 (soluble or solid phase bound), such as OKT3, and cytokines, including IL-2, for treatment of cancers and diseases of viral etiology such as those caused by HIV, cytomegalovirus and Epstein Barr virus (See entire document, especially, Column 3, lines 32-50, Column 7, lines 54-68, Column 8, lines 1-35, Column 11, lines 29-54, Column 12, lines 15-54).

Babbitt et al. teach activation of autologous T-lymphocytes (including that taken from peripheral blood of virally infected patients) with OKT3 and cytokines, including IL-2, for

treatment of tumors or viral pathogens, including herpesvirus (herpes simplex virus and cytomegalovirus), Epstein Barr virus and HIV (See entire document, especially, Column 2, lines 22-68, Column 3, Column 7, lines 40-49, Column 20, lines 53-68, Column 21, lines 1-16). It is disclosed that solid phase OKT3 may be used but that soluble OKT3 is preferred (Column 12, lines 1, 2).

Ochoa et al. (U.S. Pat. 5,443,983) teach a method of developing LAK activity in lymphocytes comprising contacting lymphocytes with IL-2 and an anti-CD3 antibody and a method of administering the same suspended in a phosphate buffered saline supplemented with human serum albumin to an AIDS patient (Column 11, lines 49-68, Column 12, lines 1-50, Claims 1-8).

Applicant acknowledges that T-cells are involved in cellular immunity against cancer and viruses (Specification, Pgs. 1, 2). Further, it is acknowledged that lymphocytes, including T-cells and NK cells, can be activated and stimulated by IL-2 and that lymphocytes can be activated and stimulated with IL-2, with or without CD3 antibodies, including against viruses, such as, EBV and CMV (Specification, pgs. 3,4).

Sekine et al. discloses that cultivation of T lymphocytes from peripheral blood lymphocytes with immobilized anti-CD3 (OKT3) and IL-2 induces a rapid proliferative response and that the immobilized form of anti-CD3 proved better for expansion than soluble anti-CD3 (Page 73, Summary, Page 74, Page 77, Discussion).

Ochoa et al. '353 discloses compositions, methods of preparing and methods of using activated autologous lymphocytes which are derived from virally infected patients and activated and proliferated by the combination of anti-CD3 antibodies in soluble or solid phase and interleukin –2, where the viral infection can be HIV, cytomegalovirus and Epstein Barr virus.

The difference between Ochoa et al. '353 and the claimed invention is that Ochoa et al. '353 does not expressly disclose excluding cytomegalovirus-infected patients, the use of anti-CD3 in solid phase or suspension in phosphate buffered saline and human albumin. However, the prior art amply suggests the same as Ochoa et al. '353 discloses the activation of autologous lymphocytes which can be used to treat viral infections, including viral infections other than cytomegalovirus, such as herpes simplex and Epstein Barr virus, which lymphocytes are activated by interleukin-2 and anti-CD3; Sekine et al. disclose that the use of solid phase anti-CD3 results in better proliferation than soluble anti-CD3; and Ochoa et al. '983 discloses the suspension of lymphocytes activated with interleukin-2 and anti-CD3 which are suspended in phosphate buffered saline and albumin. As such, it would have been well within the skill of one of ordinary skill in the art to prepare activated autologous T-lymphocytes from patients having viral infections other than cytomegalovirus, with the expectation that the activated autologous T-lymphocytes would be effective against said viral infections. Further, it would have been well within the skill of one or ordinary skill in the art to use solid phase anti-CD3 rather than soluble anti-CD3 with the expectation that suitable numbers of activated lymphocytes could be obtained at a faster rate. Finally, it would have been well within the skill of one of ordinary skill in the art to administer the activated autologous lymphocytes in a carrier containing phosphate buffered saline and albumin with the expectation that the same would be a suitable carrier.

The Applicant's arguments have been duly considered but they are deemed unpersuasive for the reasons of record and the further reasons below.

The Supreme Court in *KSR International Co. v. Teleflex Inc.*, held the following:

(1) the obviousness analysis need not seek out precise teachings directed to the subject matter of the challenged claim and can take into account the inferences and creative steps that one of ordinary skill in the art would employ;

(2) the obviousness analysis cannot be confined by a formalistic conception of the words teaching, suggestion and motivation, or by overemphasis on the importance of published articles and the explicit content of issued patents;

(3) it is error to look only the problem the patentee was trying to solve-any need or problem known in the filed of endeavor at the time of invention and addressed by the prior art can provide a reason for combining the elements in the manner claimed;

(4) it is error to assume that one of ordinary skill in the art in attempting to solve a problem will be led only to those elements of prior art designed to solve the same problem-common sense teaches that familiar items may have obvious uses beyond their primary purposes, and in many cases one of ordinary skill in the art will be able to fit the teachings of multiple patents together like pieces of a puzzle (one of ordinary skill in the art is not automaton);

(5) it is error to assume that a patent claim cannot be proved obvious merely by showing that the combination of elements was "obvious to try". *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1396, 1397 (U.S. 2007).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one

or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

The Applicant argues that Ochoa '353 does not have an enabling disclosure of treatment of virus. However, the Applicant provides no evidence that Ochoa '353 in view of the other prior art would not enable one of ordinary skill in the art to activate autologous T-cells obtained from peripheral blood of a virally infected patient using IL-2 and solid anti-CD3, suspend the same in phosphate buffered saline and human albumin and reinfuse the same into said patient for treatment of the viral infection. The rejection herein is based on a combination of references. As such, the mere fact that Ochoa '353 does explicitly disclose one or more of the steps of the claimed invention does not overcome the rejection.

The Applicant's arguments as to Santamaria and Wallace are moot as the rejection no longer relies on the same.

The Applicant argues that Babbit does not provide an enabling disclosure. However, the Applicant provides no evidence that Babbit, in view of the prior art, does not provide an enabling disclosure. The prior art, as indicated above, teaches activation of autologous T-cells, teaches obtaining the same from the peripheral blood, teaches treatment of viruses, including EBV and herpes, and teaches suspension of the activated T-cells in phosphate buffered saline and human albumin, and teaches administration of the same to a virally infected patient. As such, the combined teachings of the prior art disclose and/or suggest the claimed invention. As the Applicant's unsupported conclusion that Ochoa '353 and Babbit are non-enabling is without merit and does not overcome the rejection herein.

The Applicant argues that Sekine does not disclose or suggest treatment of virus and there would be no motivation to combine Sekine with Ochoa '353. However, under the holding in KSR, motivation is not a requirement of a *prima facie* case of obviousness. The mere fact that Sekine relates to cancer does not overcome the rejection. Sekine is being cited to show solid phase anti-CD3 is more effective than soluble anti-CD3. As indicated above, relative to the holding in KSR, one of ordinary skill in the art can look to art which not specifically directed to the problem the inventor was trying to solve and that common sense teaches that familiar items may have obvious uses beyond their primary purposes. The prior art as indicated above already teaches that solid-anti CD3 and soluble ant-CD3 are used in the art to activate T-cells whether they be from cancer patients or virally infected patients. As such, the one of ordinary skill in the art when looking to activation of autologous T-cells would look to Sekine as a reason for choosing solid phase anti-CD3 over soluble anti-CD3.

The Applicant argues that there is no motivation to combine Ochoa '983 with Ochoa '353. However, as indicated above, there is no requirement for motivation to establish a *prima facie* case of obviousness. Ochoa '983 is being cited for the teaching of suspending activated T-cells in phosphate buffered saline and human albumin. The Applicant provides no evidence that one of ordinary skill in the art would not be able to use said teaching to suspend autologous activated T-cells. As indicated above, with respect to KSR, one of ordinary skill in the art is not an automaton.

The Applicant argues that that it would not be obvious to one of ordinary skill in the art to not use specific antigens in the culture medium. However, the prior art discloses using solid phase ant-CD3 and Il-2 to activate the autologous T-cells and does not require the addition of

specific antigens, as such, the prior art as indicated above discloses and/or suggests the claimed invention.

The Applicant provides no evidence that combining six references is unusual or unreasonable. Reliance on a large number of references in a rejection does not, without more, weigh against the obviousness of the claimed invention. *In re Gorman*, 933 F.2d 982, 18 USPQ2d 1885 (Fed. Cir. 1991) (Court affirmed a rejection of a detailed claim to a candy sucker shaped like a thumb on a stick based on thirteen prior art references.). In any case, the number of references is five. The Examiner points out to the Applicant that the acknowledged prior art constitutes a prior art reference and is part of the rejection.

Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

A facsimile center has been established in Technology Center 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier number for accessing the facsimile machine is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Choi whose telephone number is (571)272-0610. Examiner maintains a compressed schedule and may be reached Monday, Tuesday, Wednesday and Thursday, 6:00 am – 4:30 pm (EST).

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Johann R. Richter, can be reached at (571)272-0646. Additionally, Technology Center 1600's Receptionist and Customer Service can be reached at (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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March 18, 2009

/Johann R. Richter/
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